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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 20040302

Application Number: 09/970,020
Filing Date: October 03, 2001
Appellant(s): LIU ET AL.

Emily R. Whelan, Reg. No. 50,391
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed December 16, 2003.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

Claims 24-54 stand or fall together.

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

WO 98/40053	Glibert et al.	09-1998
4,994,276	Baichwal et al.	02-1991

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 24-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gilbert in combination with Baichwal et al. (US 4994276).

Gilbert is relied on for teaching a bi-layer tablet that has a controlled release and immediate release profile for tramadol. See Page 1, lines, 25-31; Page 2, lines 17-37; Page 3, lines 1-3, 30-37; Page 4, lines 1-3, 13-37; Page 5, lines 1-9; Page 6, lines 30-35. The composition is controlled in such a way so as to reduce the adverse side effects of nausea and/or dizziness believed to be associated with the enantiomer. See Page 5, lines 3-9. The dosage forms taught by Gilbert may be designed to release either of the enantiomers faster than the other, or before the other. See Page 3, lines 30-37; Page 4, lines 1-12. Further, the dosage forms can be formulated to deliver the drugs at a constant rate for at least 8 hours preferably 12 hours and most preferably 24 hours. See Page 3, lines 30-37. The release profiles taught in the specification and shown in the Figures teach the release profiles of the instant claims.

Still further, Gilbert teaches that any conventional controlled-release technology can be used to achieve the desired tablet formulation. Gilbert does not expressly teach the heteropolysaccharide and polysaccharide gum excipient formulation. Gilbert does not expressly teach the exact ranges recited for the release profiles and the concentrations in the instant claims.

Baichwal is relied on for teaching a free-flowing slow release excipient formulation comprising a heteropolysaccharide (xanthan gum), a polysaccharide (locust bean gum) and inert filler. See Col. 4, lines 7-67. This excipient formulation is used to achieve slow release profiles for a wide variety of drugs wherein the ratio of the drug to excipient is 1:3-7 and can be varied to achieve dissolution profiles for about 24 hours.

See Col. 9, lines 3-44. One type of drug that can be release in such a system is an analgesic. See Col. 9, line 66 – Col. 10, line 6.

Therefore, it would have been obvious to a person of ordinary skill in the art to incorporate the free-flowing slow release excipient formulation taught by Baichwal into the bi-layer tablet that has a controlled release and immediate release profile for tramadol taught by Gilbert because Gilbert teaches that any conventional controlled-release technology can be used to achieve the desired controlled release tablet formulation and Baichwal teaches a conventional controlled release excipient for delivery of an active agent over a 24 hour period. One would be motivated to use the excipient system of Baichwal for the controlled release portion of the bi-layer tablet because of its ability to be used with a wide variety of drugs, both soluble and insoluble as well as the inexpensive nature for producing a tablet with such a system. Further, the excipient system of Baichwal is inexpensive to manufacture and can be easily compressed into tablets which eliminates the use of expensive manufacturing equipment. It is the position of the Examiner that it would have been obvious to incorporate the controlled release formulation as taught by Baichwal to tablet formulation that can include any conventional components that produce a controlled release profile for up to a 24 hour period as taught by Gilbert to produce an inexpensive, easily produced tablet formulation that controls the release of tramadol enantiomers over an extended period of time.

(11) Response to Argument

Appellants argue that the Examiner has not established a prima facie case of obviousness because no motivation exists to combine the teachings of Gilbert and Baichwal. See Appeal Brief at Page 3. To support their argument, the appellants argue that Baichwal does not teach a multiple release system and Gilbert does not teach a controlled release system that includes a heteropolysaccharide and polysaccharide gum excipient. See Appeal Brief at Page 4. Further, the appellants argue that the Examiner has provided only conclusory statements as motivation to combine the reference and no specific reason why one or ordinary skill would choose the system of Baichwal for the tablets of Gilbert. See Appeal Brief at Page 4.

It is the position of the Examiner that proper motivation exists as stated above in the obvious type rejection. The primary reference, Gilbert, teaches that a bi-layer tablet of different release profiles for enantiomers of tramadol can be formed by using *any* conventional controlled-release technology to achieve the desired effect. That desired effect is to deliver the active agent enantiomers over a 24-hour period. The secondary reference, Baichwal, teaches one such conventional controlled-release technology that can be used to achieve the effect of delivering an active agent over a 24-hour period. This secondary reference further teaches that the excipient system can be used with a wide variety of drugs that are soluble and/or insoluble and that this system is less expensive and easily compressed in the preparation of the tablets. The Examiner cites these advantages as the motivation for combining the references. It is the position of the Examiner that the advantages recited are more than mere conclusory statements as

suggested by the Appellants. They are advantages of the controlled release excipient taken directly from the reference itself.

In addition, in support of the lack of motivation argument Appellants argue that over 2,000 references, if not 22,000 references, exist in the U.S. patent database since 1976 that teach a controlled release formulation and no motivation exists to choose the Baichwal formulation over any of the thousands of other systems. See Appeal Brief at Page 5.

As stated in the July 2003 Final Rejection, the Examiner finds these results very broad and unpersuasive. The Examiner does not doubt that applicants received over 2, 00, if not 22,000 hits when the recited words/terms were used as search terms. But, Appellants have not provided any evidence that all 2,061 or 22,097 references found by that search teach a controlled release system. Rather, Appellants have only shown that those three words appear in the same reference. The search of the Appellants does not show that the 2,000 references all teach controlled release systems. Many references exist within the U.S databases that may mention controlled release systems but do not actually teach an invention that ***IS*** a controlled release system. Therefore, it is the position of the Examiner that the search results recited by Appellants are not indicative of over 2,000 controlled release systems, but rather, 2,000 references that contain the terms "controlled release formulation" or "sustained release formulation" or "extended release formulation" and the term "pharmaceutical".

Again, it is the position of the Examiner that sufficient motivation exists to combine the cited references. The excipient system of Baichwal is suitable for a wide

variety of active agents, it is inexpensive and easily compressed in the production of tablets. Gilbert states that any conventional controlled release system can be utilized. Baichwal is one such system that provides the advantages listed herein.

Finally, Appellants argue that the Examiner is using improper hindsight reconstruction to formulate the obviousness rejection. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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March 3, 2004

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